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Behaviors of children with unilateral vision impairment in the Infant Aphakia Treatment Study

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Abstract

Purpose—To determine whether behavioral functioning of 4.5-year-olds differs between two treatments for unilateral cataract and whether behavioral functioning is predicted by visual acuity in the treated eye.

Methods—The Infant Aphakia Treatment Study is a multicenter clinical trial in which 114 infants with unilateral congenital cataracts were randomized to undergo cataract extraction with contact lens correction or implantation of an intraocular lens. Patching data were collected during the year preceding a visit at age 4.5 years, when both visual acuity and caregiver-reported behavioral functioning were assessed for 109 participants. Caregiver stress was assessed with the Parenting Stress Index at 4.25 years.

Results—There were no treatment group differences in behavioral functioning as measured by the Child Behavior Checklist. Poorer visual acuity was associated with more externalizing behavior problems (attention problems and aggressive behavior) and total behavior problems in regression models that did not include caregiver stress. With multiple imputation, both caregiver stress and dichotomized visual acuity significantly predicted externalizing problems.

Conclusions—Treatment assignment did not greatly affect caregiver-reported behavior. Poor visual acuity may confer risk for problems with attention and aggressive behavior in preschoolers treated for unilateral cataract.

The psychosocial effects of occlusion for amblyopia are debated. Some studies of children with amblyopia have not found a negative impact on psychosocial well-being.^{1,2} Severity of amblyopia has not been linked to behavioral functioning, although parents reported more externalizing behavior problems for children with socially noticeable strabismus than for

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those with no socially noticeable strabismus.³ In the only published study addressing this issue for children with deprivation amblyopia,⁴ 22 children treated for unilateral congenital cataract (UCC) were compared to a control group of 18 siblings. No group differences were found for developmental or behavioral problems.⁴

Interpretation of these findings is limited by small samples, variability in age, interval since patching was discontinued, and failure to assess patching compliance. Nevertheless, clinicians are encouraged to consider the social impact of amblyopia therapy in making treatment decisions.⁵ Randomized clinical trials have used a parent-completed questionnaire, the Amblyopia Treatment Index,^{6,7} to assess the effect of the treatment on the child's quality of life.^{8,9}

Preschool children treated for UCC may be at risk for behavior problems due to the burden of the patching regimens, to the cosmetic effects of strabismus, to perceived negative social attention, and/or to child or caregiver frustration related to the impact of vision impairment on functioning. Children in the Infant Aphakia Treatment Study (IATS) had delayed motor skills at 4.5 years of age,¹⁰ and the importance of motor functioning to children's social interaction has been well documented.¹¹ The IATS is a randomized, multicenter trial comparing treatment of aphakia with a primary intraocular lens (IOL) or contact lens (CL) in 114 infants with initial surgery between 1 and 7 months of age for unilateral cataract extraction. Those treated initially with an IOL required additional surgeries and had more adverse events, primarily in the first year after surgery.¹² The aims of this study were to determine whether there were differences in behavioral functioning between the treatment groups at 4.5 years of age and to examine the extent to which behavioral functioning is predicted by visual acuity. Multivariate analyses control for demographic variables, age of surgery, patching compliance, and caregiver stress, because these variables have been associated with behavioral functioning or visual acuity.

Methods

Information about the design and clinical measures of the IATS has previously been published.¹³ Only elements relevant to study aims are described here. The study was approved by the institutional review boards of all participating institutions.

Study Design

Children with an IOL were prescribed spectacles for residual refractive errors of >1 D hyperopia, >3 D myopia, or >1.5 D astigmatism. Aphakic children were prescribed a contact lens to be worn when awake. Aphakic children's refractive status was assessed at regular intervals, and they were prescribed new contact lenses when their refractive errors changed. Patching of the phakic eye was prescribed for all patients: 1 hour daily per month of age until 8 months of age, and thereafter, 50% of waking hours.

During the 4.5-year visit, monocular recognition visual acuity and ocular alignment were evaluated, followed by testing of motor skills, and assessment of stereopsis.¹² Caregivers completed the Child Behavior Checklist (CBCL). Data on caregiver stress were collected at

the 4.25-year visit and were included in analyses only if the same caregiver who completed the CBCL at the 4.5-year visit also provided caregiver stress data.

Assessment Procedures

Monocular recognition acuity was assessed using the Amblyopia Treatment Study HOTV test, as described in previous publications.¹⁴ Visual acuity measures were translated into logMAR values; a logMAR of 2.93 was assigned to children with no light perception. Binocular alignment, including manifest tropia and any latent deviation, was assessed. Children were categorized as orthotropic or strabismic.

Patching compliance was assessed using a retrospective telephone interview every 3 months and an annual prospective diary. Diaries were completed 2 months after surgery and at 14, 26, 38, and 50 months of age. The interviewers were located at the data coordinating center to minimize the possibility that the respondent would exaggerate their adherence or that the interviewer would be biased by knowledge of the child's visual acuity. The information from caregivers' diary and telephone interview reports were used to calculate the average number of hours per day that the patch was worn during the year preceding the 4.5-year visit.

Child behavior problems were assessed with the CBCL/1.5-5, which consists of 99 items that respondents rate from 0 to 2 for the child (not true, somewhat/sometimes true, very/often true) over the past 6 months. The CBCL yields 2 broad, factor-based scores, a Total Problems score (T score) and 7 empirically derived syndrome scale scores. Four of the syndrome scales (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn) comprise the Internalizing factor; 2 (Attention Problems, Aggressive Behavior), the Externalizing factor. Raw scores are converted to T scores based on the norms for the child's age and sex. A T score of 70 on the syndrome scales (>97th percentile) is in the "clinical range," suggestive of an internalizing or externalizing behavior problem. T scores corresponding to the clinical range (T score 64, >90th percentile) are lower for the Internalizing, Externalizing, and Total Problems scales because these broad scales encompass more numerous and diverse problems than each syndrome scale.¹⁵

Caregiver stress was assessed with the Parenting Stress Index (PSI),¹⁶ a 120-item self-report measure yielding a Child Domain score, a Parent Domain score (with subscales of Competence, Isolation, Attachment, Health, Role Restriction, Depression, Spouse), and a Total Stress score. The PSI is interpreted via age-based percentile scores derived from the frequency distribution of the normative sample. The PSI has established reliability and validity,¹⁷ and adequate internal consistency reliability for the IATS sample during the first 2 years of life.¹⁸ Given the conceptual overlap between Child Domain scores and the CBCL, only Parent Domain scores were used in the analyses.

Statistical Methods

The data were tested for normality by computing z scores for skewness and kurtosis ($\alpha = 0.05$).¹⁵ CBCL raw scale scores for syndrome scales were used in analyses rather than T scores to take into account the full range of variation in these scales, although T scores are presented in Table 2 for descriptive purposes. Means and standard deviations of raw scores were calculated for each of the syndrome scales by sex. These were then used to calculate

standardized scales (mean = 0, standard deviation = 1) for boys and girls, separately. T scores are not truncated for the broad band Internalizing, Externalizing and Total Problems scales; analyses using T scores for these scales yield results similar to analyses using raw scores¹⁵ and allow for inclusion of scores for both boys and girls. Therefore, T scores rather than raw scores were used in analyses of broad band CBCL scales.

The Fisher exact *t* tests were conducted ($\alpha = 0.05$, two-sided) to test for group differences in demographic variables and CBCL scores. Nonparametric statistical tests (Spearman's ρ) were used to assess the bivariate relationships between CBCL scores, demographic variables, patching, and the continuous measure of visual acuity (logMAR values) because of the skewed distribution of the data and because of the visual acuity values assigned for patients with low vision. Visual acuity of the affected eye was also dichotomized (0 = 20/200 or worse, 1 = <20/200), given that 20/200 is the accepted cutoff for determination of legal blindness in the US. Pearson correlation coefficients were used to assess relationships between dichotomized visual acuity and hypothesized covariates. Regression analyses were conducted to evaluate the contribution of dichotomized visual acuity to the three CBCL summary scores, controlling for demographic and medical variables also related to CBCL or visual acuity. Because patching data were available for only 96 participants, regression analyses were conducted with and without this variable. The regressions were then repeated for the subset with both patching and PSI data, with Parent Domain scores added to the independent variables. A final regression model utilized multiple imputation¹⁹ to account for missing data in patching and parenting stress variables.

Results

Baseline clinical characteristics of patients in the IATS have been previously published.²⁰ Of the 114 patients enrolled (Figure 1), 112 had vision testing and CBCL data. Three cases were removed from the analyses, because these patients had nonocular medical conditions that might affect perceived behavior. Of the remaining sample of 109 children, 56 had been randomized to the CL group and 53 to the IOL group.

The sample was 52% female and 86% white; 34% of the caregivers reporting that they received Medicaid. Caregivers were primarily mothers (84%), ranging in age from 21 to 46 (mean, 33). The majority of caregivers (74% mothers, 69% fathers) were reported to have vocational training, some college, or a college or graduate school degree. Children underwent cataract surgery at 28 days to 6.83 months of age (mean, 2.47 ± 1.61 months). Visual acuity in the treated eye ranged from -0.22 logMAR (20/12) to no light perception (mean, 1.06 ± 0.83 ; median, 0.90); almost half had vision 20/200 or worse. Visual acuity in the fellow eye ranged from -0.22 to 0.70 logMAR (20/12 to 20/100; mean, 0.11 ± 0.14 ; median, 0.10); 89% had acuity better than 20/40. Twenty-seven percent had orthotropic ocular alignment. Patching data were available for 96 participants. Per caregiver report, children were patched 0–10 hours daily (mean, 3.22 ± 2.50 hours) during the preceding 12 months.

There were no significant differences between the IOL and CL groups in age at surgery, sex, race, mother's education, father's education, Medicaid status, ocular alignment, or visual

acuity of either eye. There were no significant group differences in CBCL broad band or narrow band standardized scores (Table 1). Therefore, the groups were collapsed for subsequent analyses. CBCL T score means were in the average range; 2%–6% had Internalizing, Externalizing, or Total Problems scores in the clinical range, consistent with the CBCL normative sample (Table 2).

Spearman correlations between logMAR values and CBCL T scores were 0.17 for Internalizing Problems, 0.24 for Externalizing Problems, and 0.22 for Total Problems. Pearson correlation coefficients for the dichotomized visual acuity values, CBCL broad band T scores, and all other variables are given in Table 3. Higher Externalizing Problems and Total Problems scores were weakly associated with worse visual acuity and strongly associated with higher levels of caregiver stress. Better visual acuity was weakly associated with greater maternal education, absence of Medicaid status, younger age at surgery, more hours patched, and lower levels of caregiver stress.

Given missing data for maternal education and the moderate correlation between maternal education and Medicaid status ($r = 0.44$), only the Medicaid variable was retained for the regression analyses. A regression model with visual acuity, Medicaid, and age at surgery accounted for 8.7% of the variance in Externalizing Problems, with visual acuity contributing unique variance ($t = -2.52$, $P = 0.013$ [$n = 109$]). For T scores, visual acuity contributed unique variance whether number of hours patched was included in the independent variable list ($t = -1.95$, $P = 0.054$ [$n = 96$]) or not ($t = -2.18$, $P = 0.032$ [$n = 109$]), again accounting for a relatively small portion of the variance (9.4% with patching, 6.8% without). Internalizing Problems scores were not uniquely predicted by visual acuity in any of the regression models.

When Parent Domain scores were added to the independent variables, visual acuity did not significantly predict any of the CBCL summary scores. Regression models including Parent Domain scores accounted for a higher proportion of the variance in the CBCL: 30% of Externalizing Problems scores and 36% of T scores. Parent Domain scores and age at surgery each accounted for significant variance in Internalizing Problems scores; higher levels of caregiver stress and later age at surgery predicted greater caregiver-reported internalizing problems. The only independent variable contributing unique variance in Externalizing and T scores was caregiver stress. Table 4 shows the results of regression analyses for Total Problems. With multiple imputation, both caregiver stress and dichotomized visual acuity emerged as significant predictors, but only for Externalizing Problems (visual acuity: $t = -2.01$, $P = 0.047$ [$n = 109$]), with all variables accounting for 29% of the variance. Otherwise missing data had little impact on the results.

Discussion

For the IATS sample at age 4.5 years, caregiver-reported behavior was in the normal range, and there were no significant differences between children treated with an IOL versus those treated with CL. Poorer vision in the treated eye was weakly associated with attention problems and aggressive behavior, and with total behavior problems even when the influence of Medicaid status, earlier age of surgery, and patching compliance were simultaneously

considered. However, when caregiver stress was included as an independent variable in the regression equations, visual acuity no longer predicted behavioral problems, except when multiple imputation was used.

Caregiver stress was the strongest predictor of behavioral functioning for the IATS sample at 4.5 years of age. This finding is not surprising, as caregiver stress is related to child behavior problems for typically developing children.²¹ Moreover, the association between caregiver stress and child behavior problems could be due to common method variance or to an unmeasured third variable, such as family support, caregiver depression, or child temperament.

If the contribution of visual acuity to child behavior problems is better captured by caregiver stress, a number of explanations are possible. Caregivers' knowledge of poor visual acuity in the child's treated eye and vision-related functional impairments may cause anxiety that leads to perceptions of greater behavioral problems in their children, given the negative reporting bias conferred by maternal stress.²² Alternatively, caregiver stress during the child's early years could have contributed to inconsistent patching, leading to poor visual acuity and related functional impairments, which could lead to behavioral problems. Poor visual acuity makes patching efforts more stressful for caregivers, potentially yielding similar outcomes. If poor visual acuity is independently associated with behavior problems, as illustrated by the multiple imputation models, the underlying mechanism might be the child's frustration while patched or active opposition to the occlusion treatment. Consistent adherence to a prescribed patching regimen is difficult in the context of poor child cooperation.

Visual acuity was not related to internalizing behavioral problems among the IATS sample. Reduced visual acuity may be unrelated to emotional reactivity, anxious/depressed behavior, somatic complaints, or social withdrawal during the preschool years and still lead to these behaviors later in childhood, when children develop greater self-awareness, social comparison skills, and abstract thinking.

The primary study limitation is the small sample, resulting in limited power to conduct the multivariable analyses required to tease apart the mechanisms underlying the associations between visual acuity, child behavior, and caregiver stress. Another limitation is that caregiver stress data were collected at a different time than visual acuity and CBCL data. Given the relative stability of the PSI over intervals of 3–12 months,¹⁷ however, it is unlikely that PSI scores at 4.5 years would have differed greatly from those collected at 4.25 years. Finally, in the absence of a comparison group of children who have not undergone treatment for UCC, it is unclear to what extent increased behavior problems among children with poor visual acuity in one eye are due to occlusion treatment or to other factors.

Caregiver-reported behavioral functioning was in the normal range for the IATS sample at 4.5 years, and there were no significant differences between children treated with an IOL versus those treated with CL. Preschoolers with visual acuity 20/200 or worse in one eye following treatment for UCC may be at increased risk for behavior problems, compared to

those with better visual acuity, although the causal pathways underlying this relationship remain unclear.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

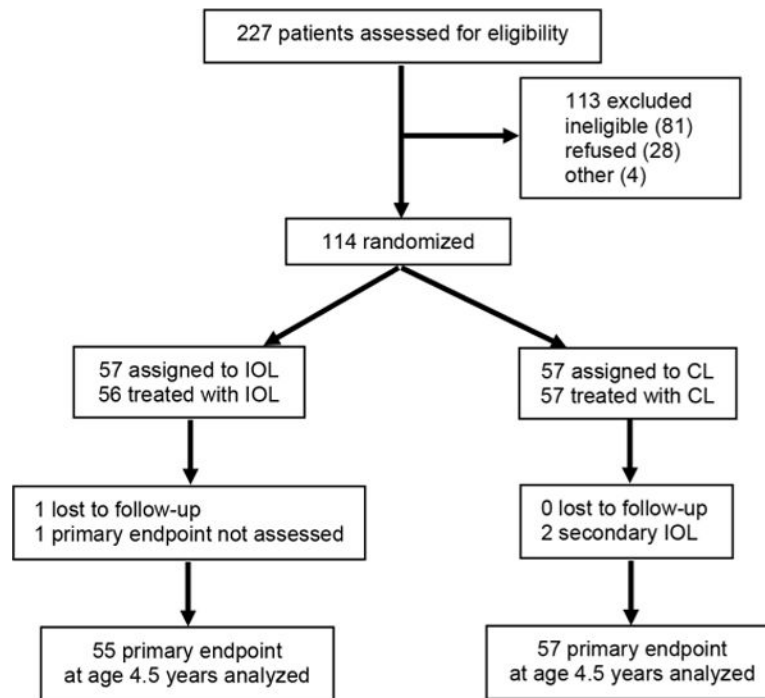
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**FIG 1.**

Consort diagram for Infant Aphakia Treatment Study. The 1 patient randomized to the IOL group but not treated was found intraoperatively to have stretching of the ciliary processes; the investigator decided that an IOL could not be safely implanted, and the patient was left aphakic and treated with a contact lens. One patient not assessed in the IOL group had developmental delay and could not complete the HOTV visual acuity test at age 4.5 years. In the contact lens group, 2 patients had a secondary IOL implanted at 1.3 and 3.0 years after randomization. A third patient had a secondary IOL implanted at 4.7 years after randomization and after the primary endpoint was assessed but before the last clinical examination at age 5 years.

Table 1

CBCL standardized raw scores by treatment group

CBCL scale	CL (n = 56), mean \pm SD	IOL (n = 53), mean \pm SD	P value
Emotionally reactive	-0.163 \pm 0.823	0.172 \pm 1.133	0.0791
Anxious/depressed	-0.117 \pm 0.812	0.124 \pm 1.153	0.2077
Somatic complaints	-0.027 \pm 0.902	0.029 \pm 1.093	0.7720
Withdrawn	-0.054 \pm 0.902	0.057 \pm 1.091	0.5606
Sleep problems	-0.004 \pm 1.015	0.004 \pm 0.984	0.9665
Attention problems	-0.096 \pm 0.809	0.101 \pm 1.160	0.3041
Aggressive behavior	-0.102 \pm 0.919	0.107 \pm 1.068	0.2750
Internalizing problems	-0.132 \pm 0.827	0.140 \pm 1.139	0.1544
Externalizing problems	-0.108 \pm 0.871	0.114 \pm 1.109	0.2481
Total problems	-0.106 \pm 0.849	0.112 \pm 1.127	0.2560

CBCL, Child Behavior Checklist; CL, contact lens; IOL, intraocular lens; SD, standard deviation.

Table 2

CBCL Total Problems (T) scores and percent in clinical range

Variable	T score ^a mean \pm SD (range)	% in clinical range ^b
Emotionally reactive	53.7 \pm 5.9 (50–70)	2%
Anxious/depressed	52.7 \pm 5.2 (50–79)	2%
Somatic complaints	52.7 \pm 4.0 (50–70)	1%
Withdrawn	53.2 \pm 4.8 (50–73)	1%
Sleep problems	53.0 \pm 5.0 (50–70)	1%
Attention problems	53.2 \pm 5.2 (50–70)	4%
Aggressive behavior	52.0 \pm 5.4 (50–88)	2%
Internalizing problems	45.2 \pm 10.8 (29–71)	6%
Externalizing problems	44.0 \pm 10.4 (28–83)	2%
Total problems	44.0 \pm 10.7 (28–76)	5%

CBCL, Child Behavior Checklist.^aT-scores are truncated at 50 for syndrome scales.^b 98th percentile for Syndrome scales, T score 64 (90th percentile) for Internalizing, Externalizing, and Total Problems scales.

Table 3

Pearson’s correlation coefficients between CBCL, dichotomized visual acuity, demographic, and medical variables

	1. Internalizing problems	2. Externalizing problems	3. Total problems	4. Maternal education	5. Medicaid	6. Age at surgery	7. Mean hours patched	8. Orthotropic	9. No. surgeries <12 mos	10. Visual acuity
1. Internalizing problems	—									
2. Externalizing problems	0.72 ^b	—								
3. Total problems	0.90 ^b	0.92 ^b	—							
4. Maternal education (n = 96)	−0.15	−0.17	−0.19	—						
5. Medicaid	0.05	0.04	0.05	−0.44 ^b	—					
6. Age at surgery	0.18	0.17	0.15	−0.04	−0.02	—				
7. Hours patched (n = 96)	−0.07	−0.15	−0.14	0.04	−0.20 ^a	−0.02	—			
8. Orthotropic (n = 108)	−0.13	−0.03	−0.05	−0.21 ^a	−0.03	0.04	−0.21 ^a	—		
9. No. surgeries <12 mos	−0.09	−0.17	−0.15	0.04	0.19	−0.19 ^a	−0.12	−0.13	—	
10. Visual acuity	−0.16	−0.27 ^b	−0.24 ^a	0.30 ^b	−0.22 ^a	−0.19 ^a	0.24 ^a	0.14	−0.09	—
11. PSI: Parent Domain (n = 87)	0.49 ^b	0.48 ^b	0.55 ^b	0.01	0.01	0.07	−0.12	0.00	−0.08	−0.16

CBCL, Child Behavior Checklist; PSI, Parenting Stress Index.

^a $p < 0.05$.

^b $p < 0.01$.

Table 4

Regression models predicting CBCL Total Problems score (T)

Independent variable	Model without caregiver stress ($R^2 = 9.4\%$; $N = 96$)			Model including caregiver stress ($R^2 = 36\%$; $N = 86$)		
	Beta	T	P value	Beta	T	P value
Intercept	45.101	14.88	0.000	18.767	3.57	<0.001
Hours patched	-0.373	-0.83	0.406	0.011	0.03	0.978
Medicaid	0.427	0.18	0.861	1.552	0.71	0.481
Age at surgery	0.892	1.33	0.188	0.874	1.47	0.145
Visual acuity dichotomized	-4.583	-1.95	0.054	-2.669	-1.25	0.213
PSI: Parent Domain				0.222	5.57	<0.001

CBCL, Child Behavior Checklist; *PSI*, Parenting Stress Index.